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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/082,502	10/19/2001	Paul O. Sheppard	97-11C2	4613

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EXAMINER	
NICKOL, GARY B	
ART UNIT	PAPER NUMBER
1642	8

DATE MAILED: 05/14/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	10/082,502	SHEPPARD ET AL.	
	Examin r	Art Unit	
	Gary B. Nickol Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the c rrespondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 February 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3 and 16-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3,16,17 and 19-24* is/are rejected.

7)☒ Claim(s) *18* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The response filed on February 24, 2003 (Paper No. 7) to the restriction requirement of December 16, 2002 has been received. Applicant has elected Group II, claims 1-5 (in part) for examination. (Because applicant did not distinctly and specifically point out any errors in the restriction requirement, the election has been treated as an election without traverse (MPEP 818.03(a).)

Claims 1-2, and 4-15 were cancelled.

Claims 16-24 were added.

Claims 3 and 16-24 are pending and are currently under examination.

Priority

With regards to Claims 3, and 16-24, SEQ ID NOs: 16-21 are accorded priority to **June 17, 1998** as being disclosed in provisional application No. 60/089,899. If applicant disagrees with any rejection of claims 3 and 16-24 set forth in this office action based on examiner's establishment of priority for the instant claims in application serial number 10/082,502, applicant is invited to submit evidence pointing to the serial number, page and line where support can be found establishing an earlier priority date.

Specification

The specification is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (i.e. see pages 61 and 62). Applicant is requested to delete all embedded hyperlinks and/or other form of browser-executable codes. See MPEP § 608.01

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3 and 23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 recites the limitation "the polypeptide". There is insufficient antecedent basis for this limitation from which claim 3 depends.

Claims 23 is vague for reciting "joined by a peptide bond to said polypeptide selected from the group...". The claim is confusing because it is not clear what "said polypeptide" is in reference to; the chimeric polypeptide? the mammalian polypeptide? Furthermore, it is not clear what DNA segment encodes the chimeric polypeptide. Is this any encoded chimeric polypeptide? Clarification is requested. See 112, 1st paragraph rejection below.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3, 19-21, and 23-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an expression vector comprising:

a transcription promoter,
DNA encoding a polypeptide selected from the group consisting of SEQ ID NO: 17, 19, 20, and 21, and
a transcription terminator; or an expression vector comprising:

a transcription promoter,
DNA encoding a chimeric polypeptide wherein said polypeptide comprises an immunoglobulin Fc polypeptide joined by a peptide bond to a polypeptide selected from the group consisting of SEQ ID NO: 17, 19, 20, and 21; and a transcription terminator...

does not reasonably provide enablement for isolated polynucleotides encoding at least 15 contiguous amino acid residues of SEQ ID NO:17, 19, 20, and 21 or vectors thereof including chimeric polypeptides encoding any and all mammalian polypeptides. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *Ex parte* Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The claims are broadly drawn to isolated polynucleotides which encode at least 15 contiguous amino acid residues of SEQ ID NO:17, 19, 20 or 21 and expression vectors thereof further comprising operably linked secretory signal sequences. The claims further include expression vectors comprising DNA segments encoding a second mammalian polypeptide joined by a peptide bond to a polypeptide selected from the group consisting of SEQ ID NO: 17,19-21.

This includes a whole universe of polynucleotides that encode polypeptides which have 15 contiguous amino acids in common with either of SEQ ID NO:17, 19, 20, or 21 and or a whole universe of polynucleotides that encode any mammalian polypeptide.

The specification teaches that the polypeptides of the invention may comprise non-conservative, non-natural, and unnatural amino acid substitutions (page 20, lines 24+). The specification further teaches (page 17, line 10) that the present invention includes nucleic acid molecules that encode a polypeptide have one or more conservative amino acid changes or all allelic variants and species orthologs of the polypeptides of SEQ ID NO: 17, 19, 20-21(page 13, line 15). Further, with regards to any encoded mammalian polypeptide (Claim 23), the specification only appears to contemplate those polynucleotides encoding an affinity tag (page 3, line 35) wherein the affinity tag is an immunoglobulin Fc polypeptide.

One cannot extrapolate the teachings of the specification to the scope of the claims because the claims are broadly drawn to any *encoded* polypeptide fragment with 15 contiguous amino acids of SEQ ID NO:17, 19, and 20-21 with or without the biological properties representative of what is claimed, and applicant has not enabled all of these types of modified proteins because it has not been shown that these modified proteins are capable of functioning as that which is being disclosed.

Protein chemistry is probably one of the most unpredictable areas of biotechnology. For example, conservative replacement of a single "lysine" reside at position 118 of acidic fibroblast growth factor by "glutamic acid" led to the substantial loss of heparin binding, receptor binding and biological activity of the protein (Burgess et al., J of Cell Bio. 111:2129-2138, 1990). In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen (Lazar et al. Molecular and Cellular Biology 8:1247-1252, 1988). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein. Furthermore, the specification fails to teach what deletions, truncations, substitutions and mutations of the disclosed sequence can be tolerated that will allow the protein to function as claimed. While it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with reasonable expectation of success are limited. Certain positions in the sequence are critical to the three-dimensional structure/function relationship, and these regions can tolerate only conservative substitutions or no substitutions. Residues that are directly involved in protein functions such as binding will certainly be among the most conserved (Bowie et al. Science, 247:1306-1310, 1990, p. 1306, col.2).

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth, and it cannot be predicted from the disclosure how to use any and all

polynucleotides or vectors comprising encoded polypeptides with 15 contiguous amino acids of SEQ ID NO:17, 19, and 20-21. Therefore, in view of the lack of predictability of the prior art, the breadth of the claims and the absence of working examples, it would require undue experimentation for one skilled in the art to practice the invention as claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 16-17, 19-22 are rejected under 35 U.S.C. 102(a) as being anticipated by Yokoyama-Kobayashi, M. *et al.* (Database GenEmbl, Accession No. AB015631, Submitted June 16, 1998).

Yokoyama-Kobayashi, M. *et al.* teach an isolated polynucleotide which encodes a polypeptide selected from the group consisting of SEQ ID NO:17 and 20. The reference further includes recombinant expression in gastric adenocarcinomas cells using expression vectors (pKA1-meta-1) wherein such vectors would inherently support transcription promoters and terminators.

Claim 18 is objected to as being dependent upon a rejected base claim.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 703-305-7143. The examiner can normally be reached on M-F, 8:30-5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Gary B. Nickol, Ph.D.
Examiner
Art Unit 1642

GBN
May 12, 2003